Docket No.: NOV-11-US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Peter VON MATT *et al.*	)	
Serial No.: 10/542,175	)	Examiner: Joseph R. Kosack
Filed: July 14, 2005	)	Art Unit: 1626
For: **INDOLYLMALEIMIDE DERIVATIVES**	)	

DECLARATION OF DR. PETER VON MATT UNDER 37 C.F.R. §1.132

Commissioner for Patents
P.O.Box 1450
Alexandria, VA 22313-1450

Sir:

I, Peter von Matt, a citizen of Stans (NW, Switzerland) and resident of Biel-Benken (BL, Switzerland), hereby declare as follows:

1. I studied chemistry at the Eidgenössische Technische Hochschule (ETH Zürich) from 1985 to 1989 and received a doctorate in Chemistry in 1993 from the University of Basel in Basel, Switzerland.

2. In 1993 -1994, I was a post-doctoral fellow at the Harvard University in Cambridge, Boston, MA.

3. Since 1995, I have been employed at Novartis AG, Basel, Switzerland as a chemist in the research and development department.

4. I am one of the inventors of the invention described and claimed in the above-

captioned Application directed to "INDOLYLMALEIMIDE DERIVATIVES".

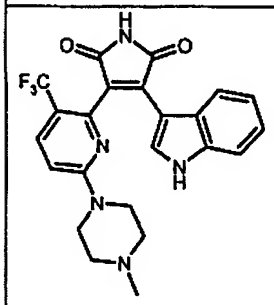
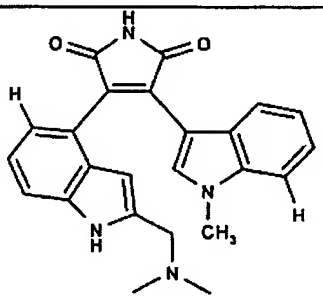
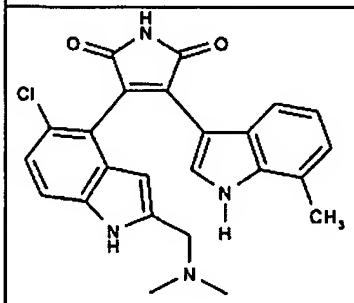
5. I have reviewed the Office Action dated Dec. 2, 2009, and the prior art reference quoted therein, WO 02/38561 (Albert et al.).

6. The present Application discloses and claims indolylmaleimide derivatives, a process for the preparation of them, pharmaceutical compositions comprising them and methods of using them. In particular, it claims the compounds of formula I wherein R is a moiety that is a substituted pyridylene moiety. This class of compounds, which are protein kinase C inhibitors and thus useful for the treatment of a number of diseases in which protein kinase C inhibitors are involved, shows certain advantages when compared with compounds carrying a bicyclic (e.g. quinoline) ring of the prior art, especially of Albert et al., WO 02/38561.

7. First, in the CD28 costimulation assay described on pages 17, line 30, to page 19, line 4 of the original description of present application Ser.-No. 10/542,175, it can be shown that already when comparing data disclosed in the application itself the monocyclic pyridyl derivatives can show superiority over bicyclic rings present in the position of R in formula I of the present application, namely the indolyl compounds. According to my considered scientific opinion, this improvement was not disclosed, suggested or even alluded to in Albert et al.

Using this test system, the following data (already disclosed in the original description) can be found for the pyridyl compound of Example 1 falling under the presently pending

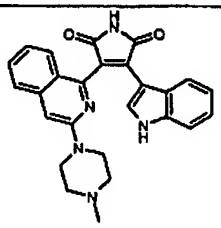
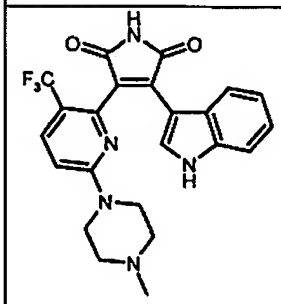
claims and the indolyl compounds of Examples 39 and 41 no longer falling under the claims:

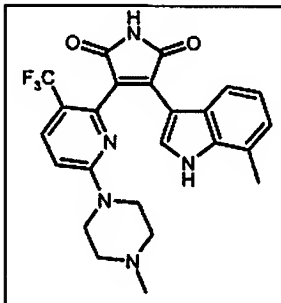
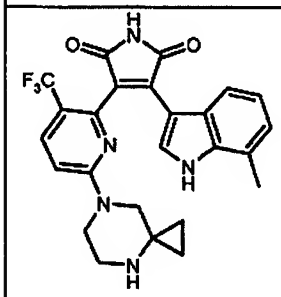
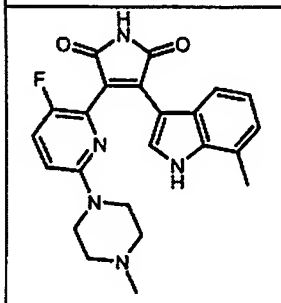
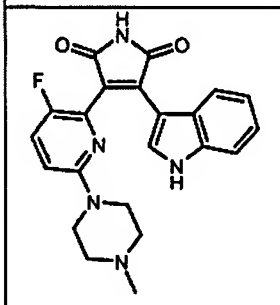
Compound	IC_{50} CD28 Costimulation (nM)	Remarks
	13.0	Compound of Example 1 of the present application, falling under the main claim and claim 12
 B	46.7	Compound of Example 39 (not claimed)
 B	28.3	Compound of Example 41 (not claimed)

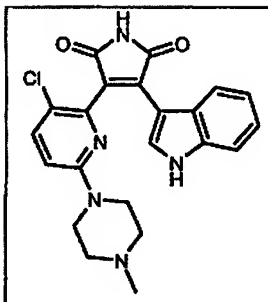
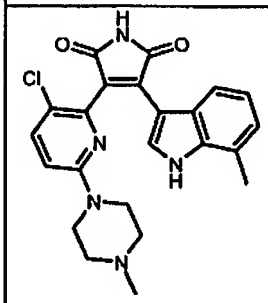
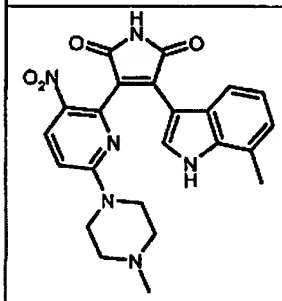
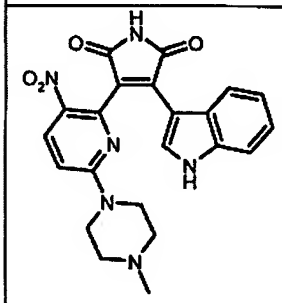
This shows that, in contrast to the opinion expressed by the Examiner in the Office Action dated Dec. 2, 1009, which stated that Albert et al. teaches monocycles versus benzofused (bi-)cycles with no loss of utility and no apparent loss of activity, the present

compound of Example 1, according to the data already shown in the description of the present application, shows a superiority. Thus this supports the view of the Examiner that claim 12 is patentable if rewritten in independent form.

8. Second and importantly, in the Mouse Mixed Lymphocyte Reaction (mMLR) assay also the compound of Example 181 in Albert et al. mentioned by the Examiner as having a quinolinylene nitrogen in the position of the pyridylene nitrogen in the present invention can be shown to be inferior to compounds of the present invention, see the following table. Said assay is described on page 19 under 9. in the original description.

Structure	Comment	MLR_M IC50 (nmol)
	Albert et al	73.3
	present invention claim 12	28.8

	present invention claim 13	22.5
		23.3
		23.5
		30.0

		18.0
		9.3
		20.8
		27.5

Thus, there is reasonable basis to conclude that due to the (regarding the binding moiety of R monocyclic) pyridylene the individual compounds mentioned in the table show a superiority over the bicyclic quinolinylene compounds of Albert et al.

It is my considered scientific opinion that Albert et al. did nor disclose or suggest such an improvement or the use of a substituted pyridylene moiety in the position of R in formula I of the present invention.

9. Albert et al. merely disclosed a number of selected and specific moieties in the position of R in formula I of the present invention. This combination, in my considered scientific opinion, did not disclose or suggest that it is not unimportant which moiety can be placed in this position.. Thus, in my considered scientific opinion, already choosing pyridyl instead of the moieties in Albert et al. was not disclosed or suggested as a viable option in said prior art document. Even more important, to my considered scientific opinion nothing there suggested or provided any allusion whatsoever to the unexpected finding that the presently claimed compounds even may be expected to show superiority based on the data mentioned above.

10. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the Application or any Patent issuing thereon.

Dated: February 15 , 2010

Peter von Matt